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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,126	04/16/2001	Randolph J. Noelle	20052/1200522-US1	4674

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,126	NOELLE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2003 and 12 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-15* is/are pending in the application.

4a) Of the above claim(s) *14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of the species IL-2 in the communication, filed 1/12/04, is acknowledged.

Claims 1 and 3-15 are pending.
Claim 12 has been canceled previously.

Claims 1-11 and 13 are being acted upon as the elected invention with respect to anti-gp39 antibodies as the gp39 antagonist, transplantation as the disease and assaying for IL-2.

Claims 14-15 have been withdrawn as being drawn to the non-elected species.

2. Upon direction to page 8 in conjunction with the original claims 6-7 and the disclosure as a whole, there appears to be sufficient antecedent basis for the instant recitation of "one to thirty days" and "from 5 - 15 days" as it applies to any gp39-/CD40L-specific antagonist .

3. Applicant's amended claim 9, filed 9/22/03, has obviated the previous rejection under 35 U.S.C. § 112, second paragraph.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The amendment filed 9/22/03, is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention.
The added material which is not supported by the original disclosure is as follows: "5,876,718" in the paragraph beginning on page 8, line 22.

Applicant is reminded that both the error and the correction need to readily apparent from the disclosure as filed when correcting the disclosure as filed.

Here, it is not readily apparent how the disclosure of "U.S. Patent No. GET 313 #" is properly corrected to "U.S. Patent No. 5,876,718".

Therefore, applicant is required to cancel the new matter in the reply to this Office Action or to provide the appropriate explanation (and appropriate evidence, if necessary) as to why this asserted correction is the obvious correction.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Upon reconsideration of applicant's amended claims, filed 9/22/03, the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Noelle et al. (U.S. Patent No. 5,876,718) has been withdrawn.

8. Claims 1-11 and 13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Noelle et al. (U.S. Patent No. 5,876,718) in view of the art known use of irradiating antigen presenting cells at the time the invention was made, as evidenced by Rooney et al. (U.S. Patent No. 5,962,318) and in view of the art known culturing of donor T cells for treatments over varying lengths of time, as evidenced by Riddell et al. (J. Immunol. Methods 128: 189-201) and monitoring the induction of T cell non-responsiveness ex vivo, as taught by Sykes et al. (U.S. Patent No. 6,006,752).

Noelle et al. teach inducing T cell non-responsiveness to desired alloantigens with gp39 antagonists, including the use of anti-gp39 antibodies (i.e. anti-CD40L antibodies) (gp39 Antagonists) and antigen presenting cells, including bone marrow and peripheral bloods cells (Cells of Induction of Antigen-Specific Tolerance), for transplantation, including bone marrow transplantation, including before transfer to the transplant recipient in vitro (Administration of Cells and gp39 Antagonists) (see entire document, including Detailed Description of the Invention). Although Noelle et al. does not mention mixed lymphocyte reaction per se, it would have readily apparent to the one of ordinary skill in the art at the time the invention was made that a mixed lymphocyte reaction was accomplished by carrying out the above-mentioned procedures. Transplantation including bone marrow transplantation are provided to recipients in need of immune reconstitution as a result of disease or disease treatment.

Although Noelle et al. is silent about the particular time ranges set recited in the instant claims 6-7 per se, one of ordinary skill would have immediately envisaged at the time the invention was made that the culture of donor T cells would have fallen into such ranges (e.g. 1, 3, 5 days), as known typical days of culturing T cells at the time the invention was made, including the Examples set forth in Noelle et al.

In addition, Riddell et al. teach the growth and expansion of antigen-specific T cells in culture for up to three months that can be employed for therapeutic use (see entire document).

Given the desired endpoint of nonresponsiveness, the ordinary artisan would have expected to culture the donor T cells, antigen presenting cells with gp39 antagonists for various times, including those encompassed by the claimed invention to achieve the desired endpoint.

It is noted that Noelle et al. teach depleting antigen presenting cells of T cells (see column 10, paragraph 2). In addition, antigen presenting cells for a variety of immunological processes were routinely irradiated at the time the invention was made to alleviate the activity of other cell types including T cells given that antigen presentation was still provided, as evidenced by Rooney et al. (e.g. see columns 14-15, overlapping paragraph and Examples 1-3 in columns 20-36).

Although Noelle et al. does not explicitly disclose monitoring or assaying ex vivo donor T cell tolerance or non-responsiveness as a separate method step, including measuring IL-2; Noelle et al. does clearly teach methods to tolerize T cells in vitro with a gp39 antagonist to affect contact dependent helper effector function (e.g. column 6, paragraph 5, column 11, paragraph 1and column 13, paragraph 3) and the Examples do exemplify various assays to monitor the induction of T cell tolerance (See Examples on columns 29).

Sykes et al. teach determining the ability of a treated T cell to release a cytokine such as IL-2 to determined the effect of an immunosuppressive drug (see entire document, particularly, column 10, paragraphs 5-6)

Given the teachings of the references, one of ordinary skill in the art at the time the invention was made would have been motivated to culture donor T cells in vitro under certain conditions and times encompassed by the claimed limitations with a gp39 / CD40 ligand antagonist such as anti-gp39 antibodies to induce antigen-specific unresponsiveness in the donor T cells populations prior to transplantation for treating various human conditions and diseases. Given the teachings of Noelle et al. and Sykes et al., one of ordinary skill in the art would have been motivated to monitor the effectiveness of the induction of T cell non-responsiveness or tolerance by treating T cells with the gp39 antagonist anti-gp39 antibodies by monitoring various parameters of T cell function, including monitoring the elaboration of cytokines, including IL-2. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

9. Upon reconsideration of the amended claims in the instant USSN 09/835,126 and copending 09/951,537, the previous provisional double patenting rejection has been withdrawn.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
April 5, 2004